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Review

Biological activities and distribution of plant saponins

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Abstract

Plant saponins are widely distributed amongst plants and have a wide range of biological properties. The more recent investigations and findings into their biological activities were summarized. Isolation studies of saponins were examined to determine which are the more commonly studied plant families and in which families saponins have been identified.

Keywords: Plant saponins; Triterpenoid; Steroidal; Biological activity; Distribution

1. Introduction

Saponins are a vast group of glycosides, widely distributed in higher plants. Their surface-active properties are what distinguish these compounds from other glycosides. They dissolve in water to form colloidal solutions that foam upon shaking (Tyler et al., 1981). Saponin containing plants are sought after for use in household detergents (*sapo*, *onis* = soap) (Bruneton, 1995). One such example is the soapwort (*Saponaria officinalis* L.), which has been widely used for centuries. Saponins have also been sought after in the pharmaceutical industry because some form the starting point for the semi-synthesis of steroidal drugs. Many have pharmacological properties and are used in phytotherapy and in the cosmetic industry. They are believed to form the main constituents of many plant drugs and folk medicines, and are considered responsible for numerous pharmacological properties (Estrada et al., 2000). Liu and Henkel (2002) consider saponins and polyphenols key ingredients in traditional Chinese medicines, and are responsible for most of the observed biological effects. For example, the ginseng root (*Panax ginseng* C.A.Meyer, Araliaceae) is one of the most important traditional oriental medicines and is now used worldwide (Fukuda et al., 2000). Saponins are said to make up the active major constituents of ginseng. The genus *Bupleurum* is officially listed in Chinese and Japanese Pharmacopoeias are used in Asian traditional medicines to treat different ailments. The dry roots of *Bupleurum fruticescens* L. (Apiaceae) are traditionally used to treat disorders associated with inflammation. The main anti-inflammatory compounds found in *Bupleurum fruticescens* are saikosaponins (Just et al., 1998). Active constituents of *Allium chinense* G.Don and *Allium macrostemon* Bunge (Alliaceae) the main sources of a Chinese Traditional medine "Xiebai" which used as a treatment for chest pain, stenocardia and cardiac asthma have been shown to be saponins (Baba et al., 2000).

Most saponins have haemolytic properties and are toxic to most cold-blooded animals. The seeds of *Barringtonia asiatica* Kurz (Lecythidaceae) which have known to contain saponins, have been used traditionally by native Asian and Pacific fisherman for centuries to enhance their catches (Herlt et al., 2002). However, since these properties are not common to all saponins, they cannot be distinguished from other compounds on the basis of these properties alone (Bruneton, 1995).

Saponins can be classified into two groups based on the nature of their aglycone skeleton. The first group consists of the steroidal saponins, which are almost exclusively present in the monocotyledonous angiosperms. The second group consists of the triterpenoid saponins, which are the most common and occur mainly in the dicotyledonous angiosperms (Bruneton, 1995). Some authors distinguish a third group called steroidal amines, which are classified by

Abbreviations: CDDP, cisplatin; ED_{50}, median effective dose; HD_{50}, haemolytic dose of 50%; HD_{100}, haemolytic dose of 100%; HGF, human gingival fibroblasts; HIV, human immunodeficiency virus; HSC, human oral squamous cell carcinoma; HSV, anti-herpes simplex virus; IC_{50}, median inhibitory concentration; LC_{50}, median lethal concentration; LD_{50}, median lethal dose; LD_{90}, lethal dose at 90%; LD_{95}, lethal dose at 95%; MIC, minimum inhibitory concentration; TGF, transforming growth factor

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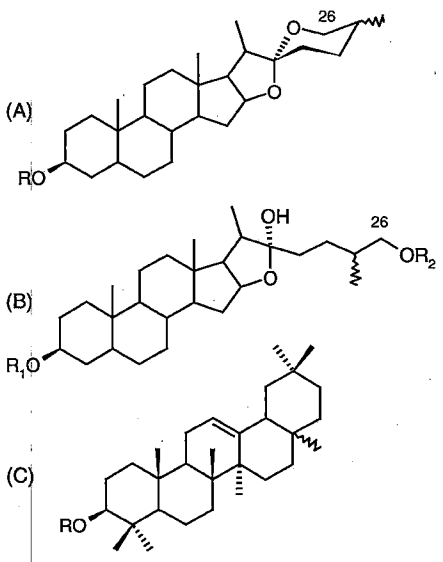

Fig. 1. Aglycone skeletons of (A) steroidal spirostane, (B) steroidal furostane, and (C) triterpenoid saponins. R = sugar moiety.

others as steroidal alkaloids (Bruneton, 1995). For the purpose of this review, only steroidal and triterpenoid saponins were considered. Steroidal saponins consist of a steroidal aglycone, a C_{27} spirostane skeleton, generally comprising of a six-ring structure (Fig. 1A). In some cases, in fresh plant material, the hydroxyl group in the 26-position is engaged in a glycosidic linkage, and so the aglycone structure remains pentacyclic. This is referred to as a furostane skeleton (Fig. 1B). Triterpenoid saponins consist of a triterpenoid aglycone, which consists of a C_{30} skeleton, comprising of a pentacyclic structure (Fig. 1C). According to Haralampidis et al. (2002), very little is known about the enzymes and biochemical pathways involved in saponin biosynthesis in plants. Haralampidis et al. (2002) review the biosynthesis of triterpenoid saponins and addressed recent advances in two key areas of saponin biosynthesis, namely the glycosylation of sapogenins and the cyclisation of 2,3-oxidosqualene.

Biological and pharmacological activities of saponins have been reported in several reviews with the most recent being Lacaille-Dubois and Wagner (1996). Similarly, this review will also summarize some of the important reports of biological active plant saponins of recent years (1998–2003) and will discuss the taxonomic distribution of recently isolated saponins.

2. Biological and pharmacological properties of saponins

2.1. Haemolytic activity

Saponins have the ability to rupture erythrocytes. This has lead to the development of the haemolytic assays for detecting the presence of saponins in drugs or plant extracts. The haemolytic properties are generally attributed to the interaction between the saponins and the sterols of the erythrocyte membrane. As a result, the membrane bursts, causing an increase in permeability and a loss of haemoglobin. Baumann et al. (2000) investigated the effect of saponins on the membrane structure through haemolysis of human erythrocytes. The findings showed that saponin-lysed erythrocytes do not reseal, and therefore indicates that saponin damage to the lipid bilayer is irreversible.

Oda et al. (2000) reported on the haemolytic activity of 47 different plant derived saponins, purified from food and medicinal plants. It has been suggested that there is a relationship between the adjuvant and haemolytic activity of saponins, however, the results indicated that the adjuvant activity does not relate with haemolytic activity. A substance or compound is said to have adjuvant activity if when used with another active compound, it enhances the activity of the active compound. The level of haemolytic activity was attributed to the type of aglycone and the presence of sugar side chains. Saponins with an acyl residue or oxide-ring moiety tended to show haemolytic activity, except for lablaboside D, which did not show haemolytic activity despite possessing a acyl residue. Escin saponins found in *Aesculus hippocastanum* L. (Hippocastanaceae) and jujuboside saponins from *Zizyphus jujuba* Mill. (Rhamnaceae) had strong haemolytic activity.

Sindambiwe et al. (1998) tested a mixture of saponins isolated from *Maesa lanceolata* Forssk. (Myrsinaceae) for haemolytic activity. The maesasaponin mixture, showed very high haemolytic activity, haemolysing 50% of the human erythrocytes (1% suspension in phosphate buffer saline) at a concentration of 1.6 μg/ml. Apers et al. (2001) also tested 10 novel saponins isolated from *Maesa lanceolata* for haemolytic activity. Some of the saponins showed no activity while others possessed very strong haemolytic activity. A number of structure–activity relationships were established and it was concluded that in the case of maesasaponins, substitution at position C-22 appears to be an essential structural feature for high haemolytic activity.

An oleanolic saponin mixture showed higher haemolytic activity than a dialysed reference saponin mixture from Merck® (HI 30 000) (Voutquenne et al., 2003). The saponins were isolated from the stem bark of *Pometia ridleyi* King emend. Radlk. (Sapindaceae). However, the quantities of pure saponins were insufficient to test individual haemolytic activities of each compound. Instead a saponin mixture was tested on sheep erythrocytes (10% suspension in phosphate buffer saline). A 70% haemolysis was obtained at 25 μg/ml. The HD_{100} was obtained at 50 μg/ml and HD_{50} was estimated at 23 μg/ml.

Ahn et al. (1998) investigated the inhibitory effect of *Bupleurum falcatum* L. (Apiaceae) saponins on anti-cell adhesive activity and its relation to haemolytic action. Saikosaponins-A, -D and -E were isolated and exhibited potent anti-cell adhesive activity and a strong haemolytic action. From the results, it was suggested that the mechanism

for anti-cell adhesive activity may resemble that for the haemolytic action.

2.2. Molluscicidal activity

Although toxic to cold-blooded species, if taken orally by warm-blooded species, saponins have only a weak toxicity (Bruneton, 1995), which is probably attributed to low absorption rates. The toxicity towards cold-blooded species has lead to the use of saponin containing drugs to catch fish.

Saponins are also highly toxic to molluscs and have been investigated as molluscicides in the control of schistosomiasis (Sindambiwe et al., 1998; Abdel-Gawad et al., 1999). *Bulinus* and *Biomphalaria* species in particular, act as intermediate hosts in the life cycle of schistosomes, which cause urinary bilharzia. Many trials have been run in African countries where schistosomiasis has a high prevalence. In a study by Sindambiwe et al. (1998) a six-oleanane-type triterpenoid saponin mixture (maesasaponin mixture, isolated from *Maesa lanceolata*) was tested for molluscicidal activity against *Biomphalaria glabrata*. The saponin mixture showed high toxicity, with LD_{95} and LD_{50} values of 4.1 and 2.3 μg/ml, respectively.

Phytolacca dodecandra L'Hér. (Phytolaccaceae) and *Phytolacca icosandra* L. berries contain saponins with highly potent molluscicidal activity (Treyvaud et al., 2000). Aqueous extracts (25 μg/ml) of *Phytolacca icosandra* had a very high molluscicidal activity against *Biomphalaria glabrata* snails. According to Treyvaud et al. (2000), the activity can be attributed to the presence of monodesmosidic saponins of serjanic and spergulagenic acids. Mølgaard et al. (2000) investigated the biodegradability of molluscicidal water-extracted saponins from the berries of *Phytolacca dodecandra*. Results showed that the saponins in an aqueous extract of *Phytolacca dodecandra* readily biodegraded ($t_{1/2}$ = 15.8 h). The saponins were completely consumed within 10 days which indicates their abilities to degrade in aquatic environments under aerobic conditions. As a result, the use of *Phytolacca dodecandra* berries for snail control in schistosomiasis-infested water bodies is environmentally acceptable.

Apers et al. (2001) tested 10 saponins isolated from the leaves of *Maesa lanceolata* for molluscicidal activity against *Biomphalaria glabrata* snails. The LC_{50} value of the saponin mixture was 1.25 mg/ml. However, it was concluded that one of the saponins, maesasaponin VI_2 is responsible for a large part of the activity of the mixture. This saponin had a LC_{50} value of 0.5 mg/ml in its isolated form.

Triterpenoid hederagenin saponins isolated from *Sapindus mukorossi* Gaertn. (Sapindaceae) had molluscicidal effects against the golden apple snail, *Pomacea canaliculata*, which have become major pests of rice and other aquatic crops throughout Taiwan and other parts of Asia (Huang et al., 2003). Seven isolated hederagenin saponins, including one new hederagenin saponin, hederagenin 3-*O*-(2,4-*O*-di-acetyl -α-L-arabinopyranoside)-(1 → 3)-α-L-rhamnopyranosyl-(1 → 2)-α-L-arabinopyranoside, resulted in 70–100% mortality at 10 ppm against the golden apple snails. Hederagenin saponins with three sugar moieties had higher molluscicidal activity than triterpene saponins with one sugar moiety.

2.3. Anti-inflammatory activity

There are a number of reports of saponins with anti-inflammatory properties. Many saponins isolated from plant sources produce an inhibition of inflammation in the mouse carrageenan-induced oedema assay. In a study by Just et al. (1998), Fruticesaponin B, a bidesmosidic saponin with an unbranched saccharide moiety isolated from *Bupleurum fruticescens* L. (Apiaceae), was shown to have the highest anti-inflammatory activity of the all the saponins tested in the mouse oedema assays. Just et al. (1998) suggested that the anti-inflammatory activity of saponins isolated from *Bupleurum fruticescens* is related to the chemical structure of the saponins. In vivo studies on saponins isolated from *Bupleurum rotundifolium* L. (Apiaceae) were reported to have anti-inflammatory activity against both 12-*O*-tetradecanoylphorbol-13-acetate (TPA) induced ear oedema and chronic skin inflammation (Navarro et al., 2001). Of the seven saponins tested, five were fairly active in reducing the TPA-induced ear oedema. The saponins produced a dose-dependent oedema reduction. Only two saponins were active in reducing the chronic skin inflammation, and also caused a parallel decrease in neutrophile infiltration.

Aescin, a mixture of triterpenoid saponins that forms the major active principle of *Aesculus hippocastanum* L. (Hippocastanaceae), has been shown to have anti-inflammatory, anti-oedematous and venotonic properties (Sirtori, 2001).

Li et al. (2002) isolated two triterpenoid saponins from the stem bark of *Kalopanax pictus* Nakai (Araliaceae). Both kalopanaxsaponin A and pictoside A were isolated and showed significant anti-inflammatory activity at the oral dose of 50 mg/ml.

A novel steroidal saponin isolated from the leaves of *Agave attenuata* Salm-Dyck (Agavaceae) was evaluated for anti-inflammatory activity using the capillary permeability assay (da Silva et al., 2002). The steroidal saponin inhibited the increase in vascular permeability caused by acetic acid which is a typical model for the first stage inflammatory reaction. However, the activity was not accompanied by an undesirable haemolytic effect and warrants further investigation as an anti-inflammatory drug.

The triterpenoid saponin loniceroside C isolated from the aerial parts of *Lonicera japonica* Thunb. (Caprifoliaceae), a medicinal plant known as an anti-inflammatory agent for centuries, showed anti-inflammatory activity when tested in vivo in the mouse ear oedema provoked by croton oil (Kwak et al., 2003). Loniceroside C inhibited the ear oedema (15–31%) at concentrations ranging from 50–200 mg/kg.

Kim et al. (1998a) investigated the anticomplementary activity of ginseng (*Panax ginseng* C.A. Mey., Araliaceae)

saponins. Ginsenoside Ro and oleanolic acid showed the highest anticomplementary activity of the tested saponins. Kim et al. (1998a) suggested that the anti-inflammatory activity of these saponins is related to anticomplementary action through the classical inflammation pathway.

2.4. Antifungal/antiyeast activity

Sindambiwe et al. (1998) tested a maesasaponin mixture isolated from *Maesa lanceolata* for its fungistatic activity. The mixture inhibited the growth of *Epidermophyton floccosum*, *Microides interdigitalis* and *Trichophyton rubrum* at a concentration of 50 μg/ml. *Candida albicans* and *Microsporum canis* growth was inhibited at 100 μg/ml. The development of *Microsporum langeroni* was inhibited at 250 μg/ml. No fungicidal activity was shown at lower concentrations up to 1 μg/ml.

Saponins isolated from *Panax notoginseng* (Burk.) F.H.Chen (Araliaceae) were reported to exhibit an inhibitory effect on *Aphanomyces cochlioides* zoospore motility (Ma et al., 1999). Seven of the 14 saponins tested had an inhibitory effect on zoospore motility.

Li et al. (1999b) tested three jujubogenin saponins isolated from *Colubrina retusa* L. (Rhamnaceae) for antifungal activity against *Candida albicans*, *Crytococcus neoformans* and *Aspergillus fumigatus*. The known saponin, jujubogenin [3-*O*-α-L-arabinofuranosyl-(1 → 2)-β-D-glucopyranosyl-(1 → 3)]-α-L-arabinopyranoside, showed modest growth-inhibitory effects with a MIC of 50 μg/ml against all three test cultures. Of the two new minor jujubogenin saponins isolated only one was marginally active with growth-inhibitory effects only against *Crytococcus neoformans* (MIC = 50 μg/ml).

In a study by Bader et al. (2000) it was shown that antifungal activity of saponins against different *Candida albicans* strains can be influenced by the variation of the etherglycosidically bonded carbohydrate units and the acylglycosidically bonded oligosaccharide at C-28 of the aglycone.

Steroidal saponins from *Yucca schidigera* Roezl. ex Ortgies (Agavaceae) (Mohave yucca) were shown to exhibit effective growth-inhibitory activities against food-deteriorating yeasts, film-forming yeasts, and dermatophytic yeasts and fungi (Miyakoshi et al., 2000). A saponin fraction, containing mainly monodesmosidic saponins, was tested for both antiyeast and antifungal activity. The saponin fraction showed growth-inhibitory activity against many of the yeasts, as well as some dermatophytic fungi (MIC values ranged between 31.3 and 125 μg/ml).

Eight previously characterized monodesmosidic saponins isolated from *Hedera colchica* K.Koch (Araliaceae) were tested for antifungal and antiprotozoal activity (Mshvildadze et al., 2000). Although the compounds exhibited antifungal activity, the activity was lower than those of the reference antifungal agents. However, even though the activity was low, there was a clear indication that the antifungal activity was structure related. Saponins with hederagenin as their aglycone were more active than those without. The number, kind and sequence of the sugar residues also had a significant effect on the antifungal activity observed.

Triterpenoid saponins from the seeds of *Chenopodium quinoa* Willd. (Chenopodiaceae) have been reported to have antifungal activity (Woldemichael and Wink, 2001). Only the crude saponin mixture inhibited the growth of *Candida albicans* at 50 μg/ml. The pure compounds showed little or no activity, which suggests a possible synergistic effect between these saponins.

Furostanol saponins isolated from the seeds of *Capsicum annuum* L. var. *acuminatum* Fingerh. (Solanaceae) showed stronger antiyeast activity than antifungal activity (Iorizzi et al., 2002). Three new furostanol saponins, capsicosides E, F and G, and seven oligoglycosides were isolated and tested for both antifungal and antiyeast activity. Antifungal MIC values ranged from 125 μg/ml to >1000 μg/ml and antiyeast MIC values from 12.5 to 10 μg/ml. However, when testing for novel pharmacological compounds, MIC values of >1000 μg/ml are generally too weak be considered active and should rather be reported as "not active".

Many different species of the genus *Phytolacca* (Phytolaccaceae) also contain saponins that show antifungal activity (Quiroga et al., 2001; Escalante et al., 2002). Three olean-type triterpenoid saponins isolated from the berries of *Phytolacca tetramera* Hauman (Phytolaccaceae) were tested for antifungal activity (Escalante et al., 2002). Two of the saponins, phytolaccosides B and E showed antifungal activity against the human pathogenic opportunistic fungi. Phytolaccoside B had the broadest spectrum of activity against the fungi tested.

CAY-1, a steroidal saponin isolated from the fruits of *Capsicum frutescens* L. (Solanaceae) was shown to be a potent fungicide and antiyeast properties (de Lucca et al., 2002). The saponins had LD_{90} values between 3 and 20 μM against various *Aspergillus* species and IC_{50} values of 9.5 μM and 6.2 μM against *Pneumocystis carinii* and *Candida albicans*, respectively. The results indicated that CAY-1 could prove to be an effective fungicide, at concentration levels that had no cytotoxic activity on A 549 lung carcinoma and HeLa cell lines.

Five new spirostanol saponins and two sterol glycosides isolated from *Solanum chrysotrichum* Schldh. (Solanaceae) leaves were tested for their antifungal activities (Zamilpa et al., 2002). One of the new spirostan saponins, 6α-*O*-β-D-xylopyranosyl-(1 → 3)-β-D-quinovopyranosyl-(25*R*)-5α-spirostan-3β,23α-ol, was the most active substance with MIC values of 100 and 200 μg/ml against *Aspergillus niger* and *Candida albicans*, respectively, and 12.5 μg/ml for both *Trichophyton mentagrophytes* and *Trichophyton rubrum*.

2.5. Antibacterial/antimicrobial activity

Saponins have also been reported to have antimicrobial activity (Killeen et al., 1998). Three butanol-extractable

5β-spirostan-3β-ol saponins were shown to have antimicrobial activity on both prokaryotic and eukaryotic organisms, but only at low cell densities. The saponins did not inhibit microbial growth of dense populations.

Three new triterpenoid saponins, Nudicaucins A, B, and C and a known saponin guaiacin D were isolated from *Hedyotis nudicaulis* Wight & Arn. (Rubiaceae) were tested against *Bacillus subtilis* (Konishi et al., 1998). All four of the isolated saponins showed weak antibacterial activity. Results indicated that the tetraglycoside saponins have stronger activity than the triglycoside saponins.

A new jujubogenin saponin isolated from *Colubrina retusa* L. (Rhamnaceae), jujubogenin 3-*O*-α-L-arabinofuranosyl-(1 → 2)-[3-*O*-(*trans*)-*p*-coumaroyl-β-D-glucopyranosyl-(1 → 3)]-α-L-arabinopyranoside, had antimycobacterial activity when tested against *Mycobacterium intracellulare* (ElSohly et al., 1999). The jujubogenin saponin had antimycobacterial activity at a MIC of 10 μg/ml.

Iorizzi et al. (2002) isolated three new furostanol saponins along with seven known saponins from the seeds of *Capsicum annuum* L. var. *acuminatum* Fingerh. (Solanaceae). The saponins showed weak or no growth inhibition against both Gram-positive and Gram-negative bacteria (MIC >1000 μg/ml).

2.6. Antiparasitic activity

Two new triterpenoid saponins, glinoside A and B, isolated from the aerial parts of *Glinus oppositifolius* L. (Molluginaceae) were shown to have antiprotozoal activity against *Plasmodium falciparum* (Traore et al., 2000). Results showed that the saponin fractions had slightly better antiplasmodial activity (IC_{50} of 31.8 μg/ml) than pure glinoside A (IC_{50} of 42.3 μg/ml).

Three saponins isolated from *Hedera helix* L. (Araliaceae), α- and β-hederin and hedeacolchiside A_1, were shown to have antileishmanial activity (Delmas et al., 2000). The results showed that these saponins exhibited a strong antiproliferative action on all the stages of development of the parasite *Leishmania infantum*. The action of the saponins was due to changes in membrane integrity and potential. Hederacolchiside A_1 had the strongest activity against both promastigote (IC_{50} of 1.2 ± 0.1 μM) and amastigote (IC_{50} of 0.053 ± 0.002 μM) form of the parasite. The same saponins also exhibited potent antiproliferative activity against human monocytes as a result of significant DNA synthesis inhibition. The findings suggest that these saponins could be considered as possible future antileishmanial drugs.

2.7. Cytotoxicity and antitumor activity

Numerous reports highlight the highly cytotoxic properties of many saponins. However, saponins with high cytotoxicity do not always have antitumor properties as cytotoxic compounds can potentially be used as antitumor agents.

A novel steroidal saponin, furcreastatin, isolated from an ethanolic extract of the leaves of *Furcraea foetida* (L.) Haw. (Agavaceae) was screened for its selective cytotoxicity towards mutant p53-expressing mouse fibroblasts (Itabashi et al., 1999). Furcreastatin consists of a hecogenin aglycone with a hexasaccharide containing D-galactose, L-rhamnose and four D-glucose residues. The compound decreased the viability of mutant p53-overexpressing cells with an ED_{50} of 4 μg/ml. Furcreastatin was also reported to be cytotoxic against parental cell-lines (ED_{50} of 9.6 μg/ml).

Many isolated steroidal saponins have been shown to be either cytostatic or cytotoxic to HL-60 human leukemia cell lines (Mimaki et al., 1998b, 1998c, 1999a, 1999c, 2001b; Yokosuka et al., 2002b). Mimaki et al. (1998b) tested 11 new saponins isolated from *Ruscus aculeatus* L. (Liliaceae). Only two of these saponins, ruscogenin diglycoside (spirostanol saponin) and its corresponding 26-glycosyloxyfurostanol saponin showed cytostatic activity at 10 μg/ml (IC_{50} values 3.1 and 3.7 μg/ml, respectively).

Mimaki et al. (1999c) also tested nine steroidal saponins, including five new saponins, isolated from the aerial parts of *Dracaena draco* L. (Dracaenaceae) for their cytostatic activities. Only two of the tested saponins showed relatively potent cytostatic activity against the human promyelocytic leukemia HL-60 cells. Only one of the new saponins, (23*S*,24*S*)-spirosta-5,25(27)-diene-1β,3β,23,24-tetrol1-*O*-[*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-(1 → 2)-α-L-arabinopyrano-syl]24-*O*-β-D-fucopyranoside, and the known compound, (25*R*)-spirost-5-en-3β-ol3-*O*-[*O*-α-L-rhamnopyranosyl-(1 → 2)-β-D-glucopyranoside], had cytostatic activities with IC_{50} values of 2.6 μg/ml and 1.3 μg/ml, respectively. Tran et al. (2001b) tested spirostanol and furostanol type saponins from the roots and rhizomes of *Dracaena angustifolia* Roxb. (Dracaenaceae) for antiproliferative activity against murine colon 26-L5 carcinoma, human HT-1080 fibrosarcoma, and B-16 BL6 melanoma cells. Three of the tested compounds showed potent antiproliferative activity against HT-1080 fibrosarcoma cells (IC_{50} values from 0.2 to 0.6 μM). Draconins A, B and C, three new steroidal saponins, were isolated from the stem bark of *Dracaena draco* along with 17 known compounds (González et al., 2003). Several of the isolated compounds showed potent cytotoxic activity against the human leukemia cell line HL-60 (IC_{50} values from 2.0 to 9.7 μM at 72 h).

Triterpenoid saponins have also shown cytotoxicity against human cell lines. A novel triterpene saponin, isolated from the root bark of *Aralia dasyphylla* Miq. (Araliaceae) showed significant cytotoxic activity against KB and HeLa-S_3 cells (Xiao et al., 1999). The IC_{50} values were 1.2 μg/ml for KB cells and 0.02 μg/ml for HeLa-S_3 cells.

Lee et al. (1999) isolated a novel saponin metabolite (IH-901) from *Panax ginseng* C.A.Meyer (Araliaceae), which showed in vitro antitumor activity. This compound was tested against four human cancer cell lines and one subline resistant to cisplatin (CDDP). From the results it was suggested that this saponin was not cross-resistant to

CDDP in the tested cell line and could be a candidate for the treatment of CDDP resistant pulmonary cancer. Ginseng saponins isolated from *Panax ginseng* C.A.Meyer (Araliaceae) and their cancer preventing activities were reviewed by Shibata (2001). It was concluded that ginsenoside, tetracyclic dammarane-type triterpenoid saponins can be administered safely as anticancer agents due to their non-toxic and non-haemolytic properties. Yun (2003) also investigated the anticancer properties of *Panax ginseng* C.A.Meyer (Araliaceae). From the study it was concluded that the activity of ginseng saponins are non-organ specific and that the anticarcinogenicity or human cancer preventative effect of *Panax ginseng* is due to the ginsenoside saponins Rg_3, Rg_5 and Rh_2.

Mimaki et al. (1999a) tested nine triterpene saponins isolated from the roots of *Pulsatilla chinensis* (Bunge) Regel (Ranunculaceae) for their cytotoxic activity. All the saponins tested exhibited moderate cytotoxic activity with IC_{50} values ranging from 2.3 to 7.8 μg/ml, with exception of one saponin which had no substituent at C-2 of the arabinosyl moiety attached to the aglycone. The results of the testing suggested that the glycoside moiety attached at the C-3 of the aglycone is essential for cytotoxic activity from the saponins evaluated.

Cytotoxic triterpenoid saponins were isolated from a methanol extract of the aerial parts of *Trevesia palmata* (Roxb. ex Lindl.) Vis. (Araliaceae) (De Tommasi et al., 2000). Six new bisdemosidic saponins, along with two know triterpenoid saponins, were tested for their antiproliferative activities against three continuous culture cell lines (J774, HEK-293 and WEHI-164). Results of this investigation showed that the hydroxyl group at C-28 and the saccharide chain esterified at C-28 play an important role in mediating antiproliferative activity.

Two new triterpenoid saponins isolated from the roots of *Acanthophyllum squarrosum* Boiss. (Caryophyllaceae) were tested in vitro for lymphocyte antiproliferation (Gaidi et al., 2000b). The results revealed one of the saponins to have a moderate concentration-dependent cytotoxic effect on lymphocytes in culture. The same saponin was not cytotoxic to lymphocytes up to a concentration of 10 μg/ml, although higher concentrations showed strong cytotoxicity.

Ginseng (*Panax ginseng* C.A.Meyer, Araliaceae) saponins were shown to have antiproliferative effects on human prostate cancer cell lines (Liu et al., 2000). One of the tested ginsenosides, ginsenoside Rg_3, displayed growth inhibitory activity against human prostate carcinoma LNCaP cells. The ginsenoside Rg_3 activated the expression of cyclin-kinase inhibitors, p21 and p27, arrested LNCaP cells at the G1 phase, and subsequently inhibited tumor cell growth through a caspase-3-mediated apoptosis mechanism.

Qiu et al. (2000) isolated the saponin chloromaloside A from *Chlorophytum malayense* Ridl. (Liliaceae), which was found to be highly cytotoxic. In vitro studies showed this steroidal saponin to have cytotoxicity against human cancer cell lines.

Julibroside J_1 and Julibroside J_9, two diastereomeric saponins isolated from the stem bark of *Albizia julibrissin* Durazz. (Leguminosae), showed cytotoxic activity (Zou et al., 2000). Both saponins showed good inhibitory action against the KB cancer cell lines in vitro. Abdel-Kader et al. (2001) tested two isolated saponins from a methanol extract of *Albizia subdimidiata* (Splitg.) Barneby & J.W. Grimes (Leguminosae) for their cytotoxic activity. Both saponins showed significant cytotoxicity against A2780 cells. One of the compounds, albiziatrioside A, is a new triterpenoid saponin and had an IC_{50} value of 0.9 μg/ml.

In a study by Yokosuka et al. (2000a) nine isolated steroidal saponins, including three new bisdesmosidic spirostanol saponins, surculosides A, B and C and one bisdesmosidic furostanol saponin, were tested for cytotoxic activity against HL-60 human promyelocytic leukemia cells. Only the three known saponins of the nine tested, showed weak cytotoxic activity with their IC_{50} values ranging from 4.2 to 8.7 μg/ml.

Eight steroidal saponins isolated from *Allium porrum* L. (Alliaceae) were found to be cytotoxic to WEHI 164 cells (IC_{50} values from 1.9 to 21.1 μg/ml) and J774 cells (IC_{50} values from 2.1 to 27.9 μg/ml) (Fattorusso et al., 2000). Three of the tested saponins had IC_{50} values below 6 μg/ml against both cell lines. Baba et al. (2000) showed saponins isolated from another *Allium* species, *Allium chinense* G.Don (Alliaceae), to have antitumor-promoting activity in a two-stage lung carcinogenesis experiment.

Two triterpene saponins, securioside A and securioside B, were isolated from a saponin fraction of an aqueous extract of *Securidaca inappendiculata* Hassk. (Polygalaceae) roots (Yui et al., 2001). The saponin fraction inhibited macrophage growth as a result of a cytotoxic effect. It was suggested that these two saponins are essential for the cell death-inducing activity of the aqueous extract.

Dong et al. (2001a, 2001b) showed steroidal saponins isolated from *Dioscorea panthaica* Prain & Burkill (Dioscoreaceae) to be cytotoxic to A375-S2, L929 and HeLa cell lines. All seven of the isolated saponins tested had cytotoxic activities against the three cell lines (Dong et al., 2001a). The IC_{50} values ranged from 8.4 to 2.2 μg/ml against A375-S2 cells, 8.6 to 1.8 μg/ml against L929 cells and 7.9 to 2.1 μg/ml against HeLa cell line. Dioscin, a known saponin had the most potent cytotoxic activity against all the cell lines (Dong et al., 2001a).

Saponins isolated from *Camassia leichtlinii* (Bak.) S. Wats. (Liliaceae) have been shown to have cytotoxic activity against human oral squamous cell carcinoma (HSC-2) cells and normal human gingival fibroblasts (Kuroda et al., 2001).

Hederagenin, ō-hederin, kalopanaxsaponin A (commonly known as α-hederin), kalopanaxsaponin I, and sapindoside C were isolated from the stem bark of *Kalopanax pictus* Nakai (Araliaceae) (Park et al., 2001). These saponins were tested for their cytotoxicity against different types of tumor cells. The results indicated that kalopanaxsaponin A has potential antitumor applications. In vivo studies on antitumor activity

by ethanol extracts of *Nigella sativa* L. (Ranunculaceae) seeds have shown the principle bioactive compound to be α-hederin, a monodesmosidic triterpene saponin (Kumara and Huat, 2001).

Mimaki et al. (2001a) tested steroidal saponins isolated from the leaves of *Cestrum nocturnum* L. (Solanaceae) for their cytotoxic activities against human oral squamous cell carcinoma (HSC-2) cells and normal human gingival fibroblasts (HGF). The steroidal saponins exhibited considerable cytotoxicity against HSC-2 cells, with LD_{50} values ranging from 2.0 to 13 μg/ml. Three of the saponins showed 5–10-fold higher cytotoxic activities against HSC-2 cells than against HGF. However, two compounds were cytotoxic against both HSC-2 cells and HGF. Mimaki et al. (2001a) concluded that the structure of the sugar portion of these steroidal saponins appears to play an important role in tumor-specific cytotoxicity.

Mimaki et al. (2001b) systematically examined the cytotoxic activities of a number of steroidal saponins isolated from plants of the Liliaceae family. Some of the saponins showed potent cytotoxic activity against HL-60 human promyelocytic leukemia cells. The cytotoxic activity was found to be linked to the monosaccharides constituting the sugar moieties and their sequences, as well as to the structure of the aglycones.

Hederacolchiside A_1, a new oleanolic acid monodesmoside isolated from *Hedera colchica* K.Koch (Araliaceae) demonstrated strong cytotoxicity activities on a number of cancer cells (IC_{50} from 4.5 to 12 μM) (Barthomeuf et al., 2002). The antiproliferative effects on the different cancer lines suggests that despite the lack of specificity for cancer cells, hederacolchiside A_1 has potential antitumor applications.

Triterpene saponins isolated from *Silene fortunei* Vis. (Caryophyllaceae) were shown to increase the accumulation and cytotoxic activity of the anticancer agent cisplatin on human colon tumor cells (Gaidi et al., 2002). On their own, the saponins did not have significant cytotoxic activities.

Four new steroidal saponins were isolated from rhizomes of *Tacca chantrieri* André (Taccaceae) (Yokosuka et al., 2002b). The isolated compounds were evaluated for their cytotoxic activity against HL-60 human promyelocytic leukemia cells. One of these compounds showed considerable cytotoxicity (IC_{50} of 1.8 μM). Two other saponins, which were structurally related to the active saponin, did not show cell growth inhibitory activity when tested at 10 μg/ml. These findings suggest that both the aglycone structure and the sugar moieties contribute to the cytotoxicity activity of the saponins. Even slight structural differences can affect the activity.

Seo et al. (2002b) isolated three new saponins and three known saponins from *Acacia tenuifolia* (L.) Willd. (Leguminosae) using bioassay-guided fractionation. The saponins showed weak activity against the genetically engineered *Saccharomyces cerevisiae* mutant (1138, 1140, 1353 and Sc-7) yeast strains tested. Two of the known saponins, which were previously isolated by Abdel-Kader et al. (2001), showed significant cytotoxic activity against M 109 lung cancer cell lines, with IC_{50} values of 1 μM. The new saponins had weak activity against the A 2780 ovarian cancer cell lines. Another *Acacia* species, *Acacia victoriae* Benth. (Leguminosae), contains saponins with tumor-inhibitory activity (Jayatilake et al., 2003). Two new saponins, Avicins D and G, were isolated from the seedpods of *Acacia victoriae*. Both compounds showed potent cytotoxic activity against human T-cell leukemia (Jurkat cells) in vitro. Avicin D and Avicin G had IC_{50} values of 0.58 μg/ml and 0.22 μg/ml, respectively. Mujoo et al. (2001) investigated the antiproliferation effect of triterpenoid saponins isolated from *Acacia victoriae*. The saponins and avicins markedly inhibited the growth of several tumor cell lines with low growth inhibition in human foreskin fibroblasts, mouse fibroblasts and immortalized breast epithelial cells at similar concentrations. Hanausek et al. (2001) tested the ability of avicin saponins from *Acacia victoriae* to inhibit chemically induced mouse skin carcinogenesis. The results suggest that these compounds could be potential suppressors of the development of human skin cancer and other epithelial malignancies. Three new saponins, isolated from the fruits of *Acacia concinna* Wall. (Leguminosae), were tested for cytotoxic activity against human HT-1080 fibrosarcoma cells (Tezuka et al., 2000). All three saponins, kinmoonosides A, B and C exhibited significant cytotoxicity with ED_{50} values of 0.7, 0.91 and 2.83 μM, respectively. It is thought that the ester moiety found at C-21 of the aglycone is not crucial for the cytotoxicity but may rather intensify the activity.

Another novel triterpenoid saponin, pittoviridoside, was isolated from *Pittosporum viridiflorum* Sims (Pittosporaceae) using bioassay-guided fractionation with genetically engineered *Saccharomyces cerevisiae* mutant yeast strains (1138, 1140, 1353 and Sc-7) (Seo et al., 2002a). The compound was shown to have both weak cytotoxicity activity against A 2780 human ovarian cancer cell lines (IC_{50} 10.1 μg/ml) and weak activity against yeast strains.

Mixtures of saponins have also been shown to have cytotoxic activities. Marquina et al. (2001) reported on a mixture of monodesmoside saponins, which were not active as pure compounds, to be highly cytotoxic against P388 and colon cell lines (ED_{50} values of 2.3 and 3.6 μg/ml, respectively).

2.8. Antiviral activity

Saponins have also been reported to have antiviral activities. Simões et al. (1999) tested two triterpenoid saponins isolated from Brazilian and Chinese plants for their antiviral activity. Both triterpenoid saponins exhibited antiviral activity. The oleanane-type inhibited herpes simplex virus type 1 DNA synthesis, while the ursane-type saponin inhibited viral capsid protein synthesis of herpes simplex virus type 1.

Triterpenoid saponins from the Fabaceae family have been reported to have anti-herpes virus activity (Kinjo et al., 2000). Anti-herpes simplex virus activity was found to be

structure related. Saponins having a glucosyl unit in the central sugar moiety seemed to show greater activity.

Triterpenoid saponins isolated from the leaves of *Maesa lanceolata* Forssk. (Myrsinaceae) were tested for structure–activity relationships against HSV-1 (for extracellular virucidal activity) and HIV viruses (Apers et al., 2001). It was concluded that a free 16-OH and acylation of the 22-OH appears to be essential for antiviral activity. These saponins, however, showed no anti-HIV activity and it was concluded that the cytotoxicity of the compounds were more pronounced than a potential antiviral effect.

Arganine C, a saponin isolated from the fruits of *Tieghemella heckelii* Pierre ex A.Chev. (Sapotaceae) was reported to have antiviral activity (Gosse et al., 2002). The saponin, strongly inhibited the entry of HIV into cells in a cell fusion assay, and showed no significant cytotoxicity towards HeLa-$CD4^+$ cells.

A mixture of tea-seed saponins from *Camellia sinensis* L. var *sinensis* (Ternstroemiaceae), were reported to inactivate human type A and B influenza viruses. However, these saponins were also toxic to the host cells and further studies need to be conducted (Hayashi et al., 1999).

The maesasaponin mixture isolated from *Maesa lanceolata* Forssk. (Myrsinaceae) was reported to have both anti-herpes simplex virus type 1 (HSV-1) and poliovirus type 1 activity (Sindambiwe et al., 1998). The saponin mixture reduced the HSV-1 infectivity at a concentration of 100 μg/ml and inactivated the Herpes simplex virus at 250 μg/ml.

Escin saponins isolated from the seeds of *Aesculus chinensis* Bunge (Hippocastanaceae) were tested for HIV-1 protease inhibition (Yang et al., 1999). Eight saponins were tested, four of which were novel compounds. The escin saponins inhibited 86.1 ± 0.2% of the HIV-1 protease activity at a concentration of 100 μM. A mixture of the saponin escin Ia and escin Ib showed 89.9 ± 1.1% inhibitory activity against HIV-1 protease at 100 μM. Escin Ia and escin Ib showed inhibitory activity against HIV-1 protease with IC_{50} values of 35 μM and 50 μM, respectively.

2.9. Other biological activities

The roots of *Panax* species (ginseng) have been found to contain a series of tetracyclic triterpenoid saponins which make up the active ingredients. The saponin content is said to vary between different *Panax* species (Nocerino et al., 2000). Ginseng saponins have been shown to have a wide variety of biological properties. The aphrodisiac and adaptogenic properties of *Panax quinquefolium* L. (Araliaceae) and *Panax ginseng* C.A.Meyer were reviewed by Nocerino et al. (2000). It was concluded that when used appropriately, ginseng appears to be safe, but side effects are documented. Attele et al. (1999) reviewed selected effects of *Panax* species and their major active steroidal saponin components. The structure-function relationship and potential targets of action were discussed. The ability of ginsenosides to independently target multireceptor systems at the plasma membrane and activate intracellular steroid receptors is thought to explain their pharmacological effects.

Saponins from Ginseng Radix rubra (*Panax ginseng* C.A.Meyer, Araliaceae) were shown to have an effect on wound healing (Kanzaki et al., 1998). The study involved examining the effects of saponin on the extracellular matrix metabolism, the activation and synthesis of TGF-β1, and the modification of TGF-β receptor expressions in fibroblasts in order to clarify the contribution of the TGF-β pathway to the mechanism of wound healing. It was concluded that saponin stimulates the wound healing process through changes of the extracellular matrix metabolism and is accompanied by modification of TGF-β receptor expressions in fibroblasts.

Huong et al. (1998a) investigated the antioxidant activity of Vietnamese ginseng (*Panax vietnamensis* Ha & Grushv., Araliaceae) saponins. The results of the study showed that Vietnamese ginseng saponins exert protective action against free radical-induced tissue injury. However, the activity is attributed to the minor saponin components rather that the major saponin components.

Korean red ginseng (*Panax ginseng* C.A.Meyer, Araliaceae) saponins were also found to have an effect on ethanol-induced amnesia (Lee et al., 2000). Jin et al. (1999) also worked on two Korean red ginseng saponins, protopanaxadiol and protopanaxatriol, and their effect in different ratios on scopolamine-induced learning ability and spatial working memory in mice. The two saponins improved the scopolamine-induced learning impairment at different dosages in the mice. However, neither of the saponins showed a favorable effect on learning and memory in normal mice. Different ratios of the two saponins were shown to have different effects. A low protopanaxadiol/protopanaxatriol ratio improved the spatial working memory of the mice. The reverse showed no improvement suggesting that the protopanaxadiol/protopanaxatriol ratio of ginseng saponins may play an important role in the pharmacological effect of red ginseng. Une et al. (2001) investigated the effect of saponins on cognitive behaviour and anxiety in albino mice. The saponin mixture isolated from *Albizzia lebbeck* Willd. (Leguminosae) significantly improved the retention ability of the normal and amnesic mice as compared to the respective controls.

Kim et al. (1998b) showed the effect of ginseng total saponin from the root of *Panax ginseng* C.A.Meyer (Araliaceae) on morphine-induced hyperactivity and conditioned place preference in mice. An intraperitoneal injection of ginseng total saponin prior to, and during the morphine treatment in mice inhibited morphine-induced hyperactivity and conditioned place preference. A single dose of ginseng total saponin also inhibited apomorphin-induced climbing behaviour which shows the antidopaminergic action of the saponins at the postsynaptic dopamine receptor.

In another study by Kim et al. (1999) the administration of ginseng total saponin prior to and during the nicotine treatment in mice inhibited, not only nicotine-induced hyperac-

tivity and conditioned place preference, but also postsynaptic dopamine receptor supersensitivity in nicotine-induced conditioned place preference mice. The results suggest that ginseng total saponin may be useful for the prevention and therapy of some of the adverse effects of nicotine.

A new oleanene-type saponin isolated from the flowers of *Spartium junceum* L. (Leguminosae) showed potent anti-ulcerogenic activity (Yeşilada and Takaishi, 1999). The saponin named spartitrioside exerted a potent effect against ethanol-induced gastric lesions in rats. The activity was more effective than the reference compound, famotidine.

Saponins isolated from *Polygala senega* L. (Polygalaceae) had potential vaccine adjuvant activity, increasing specific immune responses in mice immunized with ovalbumin and hens immunized with rotavirus (Estrada et al., 2000). The saponins increased specific antibody levels to the antigens in both the mice and hens. Saponins as potential adjuvants for orally-administered vaccines were reviewed by Sjölander and Cox (1998). Special reference was made to the induction of local and systemic immune responses and interactions with the internal epithelium. Barr et al. (1998) also reviewed the adjuvant activity of saponins. Saponins from *Quillaja saponaria* Molina (Rosaceae) and the relationships between adjuvant activity, toxicity and saponin structure were reviewed. Oda et al. (2003) also examined the relationship between adjuvant activity and saponin structure. The correlation between adjuvant activity and the amphipathic structure of soyasaponins was investigated. It is thought that the amphipathic structure may indeed define the fundamental adjuvanticity of saponins. In a brief overview by Kersten and Crommelin (2003) of iscoms which have built-in adjuvants in the form of *Quillaja* saponin, recent research on the use of better defined saponin adjuvants were discussed. According to Johansson and Lövgren-Bengtsson (1999) iscoms that are made up of different defined fractions of quillaja saponins, exhibit different immunomodulatory activities when tested for serum antibody responses.

Triterpenoid saponins from the roots and flower buds of *Panax notoginseng* (Burk.) F.H.Chen (Araliaceae) showed potent hepatoprotective effects on liver injury induced by D-galactosamine and lipopolysaccharide (Yoshikawa et al., 2003). The major saponins isolated from the buds, ginsenosides-Rb_3 and -Rc, showed stronger hepatoprotective activity than the major saponins isolated from the roots, ginsenoside-Rb_1 and -Rg_1. Sixteen triterpenoid saponins from *Panax vietnamensis* Ha & Grushv. (Araliaceae) were also found to posses hepatocytoprotective effects on D-galactosamine/tumor necrosis factor-alpha-induced cell death in primary cultured mouse hepatocytes (Tran et al., 2001a). From these results it was concluded that the hepatocytoprotective effect of Vietnamese ginseng is due to dammarane-type triterpene saponins that have an ocotillol-type side chain. Tran et al. (2002) investigated the hepatoprotective effect of majonoside R_2 the major saponin constituent from *Panax vietnamensis*. The saponin was tested in vivo on D-galactosamine/lipopolysaccharide-induced hepatic apoptosis and subsequent liver failure in mice. Majonoside R_2 was found to protect primary cultured mouse hepatocytes from cell death by inhibiting the induced apoptosis. Majonoside-R_2, was also investigated for its effect on behavioural and pathophysiological changes caused by psychological stress (Huong et al., 1998b). Majonoside-R_2 attenuated communication box paradigm-induced psychological stress (CBP stress) and conditioned fear stress-induced antinociception, and had a protective effect against CBP stress-induced gastric lesions. The saponin also restored the hypnotic activity of pentobarbital to levels similar to the unstressed controls. Saponins from different *Panax* species have been reported to demonstrate a number of actions on the central nervous system. Results from studies done on saponins isolated from *Panax japonicus* C.A.Meyer (Araliacae), indicate that these saponins may be useful in the treatment of neurodegenerative diseases (Zou et al., 2002a). Four new isolated yesanchinoside saponins together with nine ginsenosides were tested. Ginsenosides Rb_1 and Rb_4 and notoginsenosides R_4 and Fa were shown to have significant neurite outgrowth activity in human neuroblastoma SK-N-SH cells. These saponins were also found to significantly increase the total length of the neurites and the number of varicosities per cell. Ginsenosides Rb_1 and Rb_4 increased the total length of neurites by more than three times the control. Liao et al. (2002) also investigated the effect of saponins (ginseng total saponin) on neurological disorders. The neuroprotective effects of ginseng total saponin and ginenosides Rb_1 and Rg_1 on spinal cord neurons were investigated. In vitro studies revealed ginsenosides Rb_1 and Rg_1, isolated from the roots of *Panax ginseng* C.A.Meyer (Araliaceae), as efficient neuroprotective agents. The saponins protected the spinal neurons from excitotoxicity induced by glutamate and kainic acid, as well as oxidative stress induced by hydrogen peroxide. The effects were shown to be dose dependent, with the optimal dose of 20–40 μM to be most effective.

In a study by Herlt et al. (2002), two major saponins, 3-*O*-{[β-D-galactopyranosyl-(1 → 3)-β-D-glucopyranosyl(1 → 2)]-β-D-glucuronopyranosyloxy}-22-*O*-(2-methylbutyroyloxy)-15,16,28-trihydroxy-(3β,15α,16α,22α)-olean-12-ene and 3-*O*-{[β-D-galactopyranosyl(1 → 3)-β-D-glucopyranosyl(1 → 2)]-β-D-glucuronopyranosyloxy}-22-*O*-(2(*E*)-methyl-2-butenyloyloxy)-15,16,28-trihydroxy-(3β,15α,16α,22α)-olean-12-ene, were isolated from the seeds of *Barringtonia asiatica* Kurz (Lecythidaceae) and tested for antifeedant properties towards *Epilachna* larvae. The saponins were tested at concentrations of 1000, 500, 100 and 50 μg/ml on *Solanum nigrum* leaves. The results showed the saponin contaning tiglate to have considerably higher antifeedant activity than the saponin containing 2-methylbutyrate. At a concentration of 100 μg/ml, the tiglate-containing saponin had 39% antifeedant activity and the 2-methylbutyrate-containing saponin had 0% activity.

Three novel ginseng saponin metabolites formed by intestinal bacteria were evaluated for their antigenotoxic properties (Lee et al., 1998). The compounds inhibited benzopyrene-induced mutagenicity in a dose-dependent manner. It was suggested that the results indicate that these ginseng saponin metabolites could have potential as chemopreventive agents. Scarpato et al. (1998) investigated the effects of isolated saponins from *Bupleurum fruticosum* L. (Apiaceae) on the clastogenicity and cytotoxicity of the anticancer drugs mitomycin C and bleomycin. One of the saponins showed a dose-dependent mitomycin C-induced mutagenesis inhibition and a co-genotoxic effect on bleomycin-treated cultures. Soybean (*Glycine max* Merrill., Leguminosae) extracts have been shown to repress induced genomic DNA damage, cell clastogenicity and point mutation in cultured mammalian cells. Berhow et al. (2000) showed that a mixture of soyasaponins repressed 2-acetoxyacetylaminofluorene (2AAAF)-induced DNA damage in Chinese hamster ovary cells. Soyasapogenol B aglycone showed significant antigenotoxic activity against 2AAAF. These results are the first to demonstrate the antimutagenic activity of soybean saponins in mammalian cells. Yoshiki et al. (1998) reviewed the relationship between the chemical structure and biological activities of triterpenoid saponins isolated from *Glycine max* Merrill. (Leguminosae).

Saponins isolated from the roots of *Zygophyllum gaetulum* Emb. & Maire (Zygophyllaceae) were tested for their effects on electrically-stimulated guinea-pig ileum (Aquino et al., 2001). The results showed that the saponin zygophyloside N significantly reduced the electrically-induced contractions. The antispasmodic activity shown by this saponin was dose-dependent.

In a study by Parab and Mengi (2002) saponins extracted from *Acorus calamus* L. (Araceae) were tested for hyperlipidemic activity. Treatments of hyperlipidemic rats with saponins (10 mg/kg) significantly decreased the serum cholesterol and triglyceride levels. However, neither of the lipoprotein levels were brought down to baseline values, but it was still concluded that the saponins contribute to the hypolipidemic activity of *A. calamus*. Saponin fractions from *Allium* species have been shown to decrease the plasma total cholesterol levels (Matsuura, 2001). The active fractions contained steroid saponins which are thought to be responsible for the cholesterol lowering effects of garlic. In a minireview of natural products and their biological activities, saponins were listed under compounds with hypocholesterolemic activity (Wang and Ng, 1999).

3. Distribution of saponins

Saponins are found in a wide variety of foods including asparagus, beans, blackberries, peas, potatoes, sugar beet and tea (Dini et al., 2001a). They occur in many different plant families, as evidenced by the isolation of saponins from phytochemical studies of many plant species over the years. Table 1 provides a list of species from which saponins have been isolated in the last 5 years (1998–2003). Although this list is not exhaustive, it does give a good indication of the plant species and families which have formed the focus of research in saponin chemistry in recent years. Many of these species have been chosen for phytochemical research based on ethnobotanical use. Of the roughly 200 species listed, 40% of the species were investigated based their traditional usage. Two triterpenoid saponins, eliciting

Table 1
A list of plant species from which saponins have been isolated in recent years (1998–2003)

Family	Species	Saponin type	Reference
Agavaceae	*Agave americana* L.	Steroidal	Yokosuka et al., 2000a
	Agave attenuata Salm-Dyck	Steroidal	da Silva et al., 2002
	Agave decipiens Baker	Steroidal	Abdel-Gawad et al., 1999
	Cordyline stricta (Sims) Endl.	Steroidal	Mimaki et al., 1998d
	Furcraea foetida (L.) Haw.	Steroidal	Itabashi et al., 1999
	Yucca filamentosa L.	Steroidal	Plock et al., 2001
	Yucca schidigera Roezl. ex Ortgies	Steroidal	Miyakoshi et al., 2000
			Oleszek et al., 2001
Alliaceae	*Allium chinense* G.Don	Steroidal	Baba et al., 2000
	Allium karataviense Regel	Steroidal	Mimaki et al., 1999b
	Allium nutans L.	Steroidal	Akhov et al., 1999
	Allium porrum L.	Steroidal	Carotenuto et al., 1999
			Fattorusso et al., 2000
	Allium triquetrum L.	Steroidal	Corea et al., 2003
	Allium tuberosum Rottl. ex Spreng.	Steroidal	Sang et al., 1999a, 1999b, 2001a, 2001b
			Zou et al., 2001

Table 1 (*Continued*)

Family	Species	Saponin type	Reference
Amaranthaceae	*Achyranthes aspera* L.	Triterpenoid	Kunert et al., 2000 Michl et al., 2000
	Achyranthes bidentata Blume	Triterpenoid	Mitaine-Offer et al., 2001a, 2001b
	Alternanthera repens (L.) Link	Triterpenoid	Sanoko et al., 1999
	Amaranthus caudatus L.	Triterpenoid	Rastrelli et al., 1998
	Amaranthus cruentus L.	Triterpenoid	Junkuszew et al., 1998 Oleszek et al., 1999
Apiaceae (Umbelliferae)	*Bupleurum falcatum* L.	Triterpenoid	Ahn et al., 1998
	Bupleurum fruticescens L.	Triterpenoid	Just et al., 1998
	Bupleurum rigidum L.	Triterpenoid	Sánchez-Contreras et al., 1998, 2000
	Bupleurum rotundifolium L.	Triterpenoid	Navarro et al., 2001 Fujioka et al., 2003
	Bupleurum scorzonerifolium Willd.	Triterpenoid	Li et al., 1999a
	Centella asiatica (L.) Urb.	Triterpenoid	Matsuda et al., 2001
Aquifoliaceae	*Ilex amara* (Vell.) Loes.	Triterpenoid	de Andrade et al., 2002
	Ilex kudincha C.J.Tseng	Triterpenoid	Nishimura et al., 1999
	Ilex latifolia Thunb.	Triterpenoid	Huang et al., 2001a, 2001b Ouyang et al., 1998
Araliaceae	*Acanthopanax nipponicus* Makino	Triterpenoid	Miyakoshi et al., 1999
	Aralia dasyphylla Miq.	Triterpenoid	Xiao et al., 1999
	Aralia elata (Miq.) Seem.	Triterpenoid	Song et al., 2000, 2001
	Cussonia bancoensis Aubrev. & Pellegr.	Triterpenoid	Tapondjou et al., 2003
	Cussonia racemosa Baker	Triterpenoid	Harinantenaina et al., 2002
	Hedera colchica K.Koch	Triterpenoid	Delmas et al., 2000 Mshvildadze et al., 2000, 2001 Barthomeuf et al., 2002
	Hedera helix L.	Triterpenoid	Delmas et al., 2000 Bedir et al., 2000
	Kalopanax pictus Nakai	Triterpenoid	Park et al., 2001 Li et al., 2002 Choi et al., 2002
	Meryta lanceolata Forst.	Triterpenoid	Melek et al., 2003
	Panax ginseng C.A.Mey.	Triterpenoid	Dou et al., 2001
	Panax japonicus C.A.Mey.	Triterpenoid	Zou et al., 2002a, 2002b
	Panax notoginseng (Burk.) F.H.Chen	Triterpenoid	Ma et al., 1999 Yoshikawa et al., 2001, 2003
	Panax pseudo-ginseng Wall.	Triterpenoid	Tanaka et al., 2000
	Panax vietnamensis Ha & Grushv.	Triterpenoid	Huong et al., 1998b Tran et al., 2001a, 2002
	Polyscias fruticosa (L.) Harms [= *Panax fruticosum* L.; *Nothopanax fruticosum* Miq.]	Triterpenoid	Huan et al., 1998
	Schefflera leucantha R.Vig.	Saponin mixture	Witthawaskul et al., 2003
	Trevesia palmata (Roxb. ex Lindl.) Vis.	Triterpenoid	De Tommasi et al., 2000
	Tupidanthus calyptratus Hook.f. & Thoms.	Triterpenoid	Cioffi et al., 2001

Table 1 (*Continued*)

Family	Species	Saponin type	Reference
Asclepiadaceae	*Gymnema sylvestre* R.Br.	Triterpenoid	Ye et al., 2000, 2001
Asparagaceae	*Asparagus africanus* Lam.	Steroidal	Debella et al., 1999
	Asparagus dumosus Baker	Steroidal	Ahmad et al., 1998
Asteraceae	*Aspilia montevidensis* (Spreng.) Kuntze	Steroidal	Bellini et al., 1999
	Aster ageratoides Turcz. var. *ovatus* Nakai	Triterpenoid	Sakai et al., 1999
	Celmisia spectablilis Hook.f.	Triterpenoid	Ueckert et al., 1998
	Conyza blinii Lévl.	Triterpenoid	Su et al., 2001, 2003
	Viguiera decurrens A.Gray	Triterpenoid	Marquina et al., 2001
Balanitaceae	*Balanites aegyptiaca* Del.	Steroidal	Kamel, 1998
Berberidaceae	*Bongardia chrysogonum* (L.) Boiss.	Triterpenoid	Atta-ur-Rahman et al., 2000
	Caulophyllum thalictroides (L.) Michx.	Triterpenoid	Jhoo et al., 2001
Buddlejaceae	*Buddleja scordioides* HBK.	Triterpenoid	Avila and Romo de Vivar, 2002
Cactaceae	*Isolatocereus dumortieri* Br. & R. [= *Isolatocereus dumortieri* Backeb.]	Triterpenoid	Kinoshita et al., 2000
Campanulaceae	*Platycodon grandiflorum* A.DC.	Triterpenoid	Nikaido et al., 1999
Caprifoliaceae	*Lonicera bournei* Hemsl.	Triterpenoid	Xiang et al., 2000
	Lonicera japonica Thunb.	Triterpenoid	Kwak et al., 2003
Caryophyllaceae	*Acanthophyllum squarrosum* Boiss. [= *Acanthophyllum pungens* (Bunge) Boiss. var. *squarrosum* Golenk.]	Triterpenoid	Gaidi et al., 2000b, 2001b
	Arenaria filicaulis Boiss. [= *Gypsophila filicaulis* (Boiss.) Borm]	Triterpenoid	Elgamal et al., 1998
			Soliman et al., 1999, 2001
	Arenaria juncea M.Bieb.	Triterpenoid	Gaidi et al., 2001a
	Gypsophila bermejoi G.López	Triterpenoid	Acebes et al., 1998a, 1998b
	Polycarpon succulentum J.Gay	Triterpenoid	Meselhy, 1998
	Saponaria officinalis L.	Triterpenoid	Jia et al., 1998b, 1999
			Koike et al., 1999a
	Silene cucubalus Wibel	Triterpenoid	Larhsini et al., 2003
	Silene fortunei Vis.	Triterpenoid	Lacaille-Dubois et al., 1999a, 1999b
			Gaidi et al., 2002
	Silene vulgaris (Moench) Garcke [= *Silene inflata* Sm.]	Triterpenoid	Glensk et al., 1999
	Spergularia ramosa Cambess.	Triterpenoid	De Tommasi et al., 1998
	Vaccaria segetalis (Neck.) Garcke [= *Vaccaria pyramidata* Medik.]	Triterpenoid	Jia et al., 1998a
			Koike et al., 1998
			Yun et al., 1998
			Ma et al., 2001

Table 1 (*Continued*)

Family	Species	Saponin type	Reference
Chenopodiaceae	*Beta vulgaris* L.	Triterpenoid	Murakami et al., 1999a
	Chenopodium album L.	Triterpenoid	Lavaud et al., 2000
	Chenopodium ficifolium Sm.	Triterpenoid	Gohar et al., 2002
	Chenopodium quinoa Willd.	Triterpenoid	Dini et al., 2001a, 2001b
			Woldemichael and Wink, 2001
			Dini et al., 2002
			Zhu et al., 2002
Combretaceae	*Pteleopsis hylodendron* Mildbr.	Triterpenoid	Ngounou et al., 1999
Cucurbitaceae	*Cucurbita foetidissima* H.B. & K. [= *Cucurbita perrenis* A.Gray; *Cucumis perrenis* E.James]	Triterpenoid	Gaidi et al., 2000a
	Cyclanthera pedata Schrad.	Triterpenoid	De Tommasi et al., 1999
	Momordica charantia L.	Triterpenoid	Murakami et al., 2001a
Diapensiaceae	*Berneuxia thibetica* Decne.	Triterpenoid	Wang et al., 1998
Dioscoreaceae	*Dioscorea panthaica* Prain & Burkill	Steroidal	Dong et al., 2001a, 2001b
	Dioscorea pseudojaponica Yamamoto	Steroidal	Yang et al., 2003
Dipsacaceae	*Scabiosa rotata* M.Bieb.	Triterpenoid	Baykal et al., 1998
Dracaenaceae	*Dracaena angustifolia* Roxb.	Steroidal	Tran et al., 2001b
	Dracaena concinna Kunth	Steroidal	Mimaki et al., 1998e
	Dracaena draco L.	Steroidal	Mimaki et al., 1999c
			González et al., 2003
	Dracaena surculosa Lindl.	Steroidal	Yokosuka et al., 2000b, 2002a
	Sansevieria cylindrica Boj.	Steroidal	Antunes et al., 2003
Eupteleaceae	*Euptelea polyandra* Sieb. & Zucc.	Triterpenoid	Yoshikawa et al., 2000b
			Murakami et al., 2001b
Hippocastanaceae	*Aesculus chinensis* Bunge	Triterpenoid	Yang et al., 1999
			Zhang et al., 1999a
			Zhao et al., 2001
Lamiaceae	*Becium grandiflorum* (Lam.) Pichi-Serm. var. *obovatum* (E.Mey. ex Benth) Sebald	Triterpenoid	Burger et al., 1998
Lardizabalaceae	*Holboellia fargesi* Reaub.	Triterpenoid	Fu et al., 2001
Lecythidaceae	*Barringtonia asiatica* Kurz	Triterpenoid	Herlt et al., 2002
	Foetidia africana Verdc.	Triterpenoid	Crublet et al., 2002
	Petersianthus macrocarpus (P.Beauv.) Liben	Triterpenoid	Olugbade et al., 2000
Leguminosae	*Acacia concinna* Wall.	Triterpenoid	Tezuka et al., 2000
	Acacia tenuifolia (L.) Willd.	Triterpenoid	Seo et al., 2002b
	Acacia victoriae Benth.	Triterpenoid	Hanausek et al., 2001

Table 1 (*Continued*)

Family	Species	Saponin type	Reference
			Mujoo et al., 2001
			Jayatilake et al., 2003
	Albizia gummifera C.A.Sm.	Triterpenoid	Debella et al., 2000
	Albizia julibrissin Durazz.	Triterpenoid	Zou et al., 2000
	Albizia lebbeck Willd.	Saponin mixture	Une et al., 2001
	Albizia myriophylla Benth.	Triterpenoid	Yoshikawa et al., 2002
	Albizia procera Benth.	Triterpenoid	Yoshikawa et al., 1998
	Albizia subdimidiata (Splitg.) Barneby & J.W.Grimes	Triterpenoid	Abdel-Kader et al., 2001
	Astragalus kahiricus DC.	Triterpenoid	Verotta et al., 2002
	Astragalus trigonus DC.	Triterpenoid	Shaker et al., 2001
	Baptisia australis (L.) R.Br.	Triterpenoid	Udayama et al., 1998
	Gleditsia sinensis Lam.	Triterpenoid	Zhang et al., 1999b, 1999c, 1999d
	Gliricidia sepium (Jacq.) Walp.	Triterpenoid	Kojima et al., 1998
	Gliricidia sepium (Jacq.) Steud.		Rastrelli et al., 1999
	Lathyrus japonicus Willd. [= *Lathyrus maritimus* Bigel.]	Triterpenoid	Kang et al., 1998
	Lupinus oreophilus Phil.	Triterpenoid	Woldemichael et al., 2003
	Medicago sativa L.	Triterpenoid	Bialy et al., 1999
	Spartium junceum L.	Triterpenoid	Yeşilada and Takaishi, 1999
	Swartzia schomburgkii Benth. var. *schomburgkii*	Triterpenoid	Abdel-Kader et al., 2000
	Trifolium spp.	Triterpenoid	Oleszek and Stochmal, 2002
	Trifolium resupinatum L.	Triterpenoid	Simonet et al., 1999
	Trigonella foenum-graecum L.	Steroidal	Murakami et al., 2000a
	Vigna angularis (Willd.) Ohwi & H.Ohashi	Triterpenoid	Iida et al., 1999
Liliaceae	*Camassia leichtlinii* (Bak.) S.Wats.	Steroidal	Kuroda et al., 2001
	Chlorophytum malayense Ridl.	Steroidal	Qiu et al., 2000
	Hemerocallis fulva L. var. *kwanso*	Steroidal	Konishi et al., 2001
	Hosta sieboldii (Paxton) I.Ingram	Steroidal	Mimaki et al., 1998c
	Lilium candidum L.	Steroidal	Haladova et al., 1998
			Mimaki et al., 1999e
	Polygonatum zanlanscianense Pamp.	Steroidal	Wang et al., 2001
	Ruscus aculeatus L.	Steroidal	Mimaki et al., 1998a, 1998b, 1999d
	Ruscus colchicus Yeo	Steroidal	de Combarieu et al., 2002
	Ruscus hypoglossum L.	Steroidal	de Combarieu et al., 2002
	Tupistra wattii Hook.f.	Steroidal	Shen et al., 2003
Lythraceae	*Lafoensia glyptocarpa* Koehne	Triterpenoid	de Carvalho et al., 1999
Menispermaceae	*Diploclisia glaucescens* (Bl.) Diels [= *Cocculus macrocarpus* Wight & Arn.]	Triterpenoid	Jayasinghe et al., 2003
Molluginaceae	*Glinus lotoides* L. var. *dictamnoides* [= *Glinus dictamnoides* Burm.f.; *Mollugo glinus* A.Rich]	Triterpenoid	Hamed and El-Emary, 1999
	Glinus oppositifolius L.	Triterpenoid	Traore et al., 2000
	Mollugo spergula L.	Triterpenoid	Sahu et al., 2001

Table 1 (*Continued*)

Family	Species	Saponin type	Reference
Myrsinaceae	*Ardisia crenata* Roxb.	Triterpenoid	Koike et al., 1999b
	Ardisia mamillata Hance	Triterpenoid	Huang et al., 2000a, 2000b
	Maesa japonica (Thunb.) Mor. & Zoll.	Triterpenoid	Koike et al., 1999c
	Maesa lanceolata Forssk. var. *golungensis* Welw.	Triterpenoid	Sindambiwe et al., 1998 Apers et al., 1999, 2001
	Maesa laxiflora Pitard	Triterpenoid	Jiang et al., 1999
	Maesa tenera Mez	Triterpenoid	Koike et al., 2001
Passifloraceae	*Passiflora edulis* Sims	Triterpenoid	Yoshikawa et al., 2000a
Phytolaccaceae	*Phytolacca dioica* L.	Triterpenoid	Soliman et al., 2001
	Phytolacca dodecandra L'Hér.	Saponin mixture	Mølgaard et al., 2000
	Phytolacca icosandra L.	Triterpenoid	Treyvaud et al., 2000
	Phytolacca tetramera Hauman	Triterpenoid	Escalante et al., 2002
Pittosporaceae	*Pittosporum viridiflorum* Sims	Triterpenoid	Seo et al., 2002a
Polygalaceae	*Carpolobia alba* G.Don.	Triterpenoid	Mitaine-Offer et al., 2002
	Carpolobia lutea G.Don.	Triterpenoid	Mitaine-Offer et al., 2002
	Polygala amarella Crantz	Triterpenoid	Desbéne et al., 1999
	Polygala senega L.	Triterpenoid	Estrada et al., 2000
	Securidaca inappendiculata Hassk.	Triterpenoid	Yui et al., 2001
Primulaceae	*Cyclamen coum* mill.	Triterpenoid	Yayli et al., 1998
Ranunculaceae	*Cimicifuga foetida* L.	Triterpenoid	Zhu et al., 2001
	Clematis tangutica (Maxim.) Korsh.	Triterpenoid	Zhong et al., 2001
	Clematis tibetana Kuntze	Triterpenoid	Kawata et al., 2001
	Eranthis cilicica Schott & Kotschy	Triterpenoid	Watanabe et al., 2003
	Nigella sativa L.	Triterpenoid	Kumara and Huat, 2001
	Pulsatilla chinensis (Bunge) Regel	Triterpenoid	Mimaki et al., 1999a
	Pulsatilla patens Mill var. *multifida* (Pritz.) S.H.Li & Y.H.Huang	Triterpenoid	Ye et al., 1999
	Thalictrum minus L.	Triterpenoid	Gromova et al., 1998
Rhamnaceae	*Colubrina retusa* L.	Triterpenoid	ElSohly et al., 1999 Li et al., 1999b
	Zizyphus joazeiro Mart.	Triterpenoid	Schühly and Heilmann, 2000
	Zizyphus jujuba Mill. var. *spinosa* Hu.	Triterpenoid	Matsuda et al., 1999
Rosaceae	*Quillaja saponaria* Molina	Triterpenoid	Guo et al., 1998, 2000 Guo and Kenne, 2000a, 2000b Marciani et al., 2001
	Rubus pungens Camb. var. *oldhamii* Maxim.	Triterpenoid	Wang et al., 2000
Rubiaceae	*Galium rivale* (Sibth. & Sm.) Griseb.	Triterpenoid	de Rosa et al., 2000a, 2000b
	Hedyotis nudicaulis Wight & Arn.	Triterpenoid	Konishi et al., 1998
	Isertia pittieri (Standl.) Standl.	Triterpenoid	Um et al., 2001
	Randia formosa K.Schum.	Triterpenoid	Sahpaz et al., 2000
	Rudgea viburnoides (Cham.) Benth.	Triterpenoid	Young et al., 1998

Table 1 (*Continued*)

Family	Species	Saponin type	Reference
Sapindaceae	*Elattostachys apetala* (Labill.) Radlk. [= *Elattostachys falcata* (A. Gray) Radlk.]	Triterpenoid	Lavaud et al., 2001
	Filicium decipiens Thwaites	Triterpenoid	Lavaud et al., 1998
	Harpullia austro-caledonica Boull.	Triterpenoid	Voutquenne et al., 2002
	Harpullia cupanioides Roxb.	Triterpenoid	Voutquenne et al., 1998
	Harpulia ramiflora Radlk.	Triterpenoid	Dizes et al., 1998
	Koelreuteria paniculata Laxm.	Triterpenoid	Soliman et al., 2001
	Pometia ridleyi King emend. Radlk.	Triterpenoid	Voutquenne et al., 2003
	Sapindus emarginatus Vahl.	Triterpenoid	Kanchanapoom et al., 2001
	Sapindus mukorossi Gaertn.	Triterpenoid	Huang et al., 2003
Sapotaceae	*Argania spinosa* (L.) Skeels	Triterpenoid	Alaoui et al., 2002
	Gambeya boukokoensis Aubrev. & Pellegr.	Triterpenoid	Wandji et al., 2003
	Madhuca longifolia (L.) Macbride [= *Bassia longifolia* L.]	Triterpenoid	Yoshikawa et al., 2000c
	Tieghemella heckelii Pierre ex A.Chev.	Triterpenoid	Gosse et al., 2002
Scrophulariaceae	*Bacopa monniera* Wettst.	Triterpenoid	Pawar et al., 2001
Solanaceae	*Capsicum annuum* L. var. *acuminatum* Fingerh.	Steroidal	Iorizzi et al., 2002
	Capsicum frutescens L.	Steroidal	de Lucca et al., 2002
	Cestrum nocturnum L.	Steroidal	Mimaki et al., 2001a
	Cestrum sendtnerianum Mart. Ex Sendt.	Steroidal	Haraguchi et al., 1999, 2000
	Lycopersicon esculentum Mill.	Steroidal	Fujiwara et al., 2003
	Solanum chrysotrichum Schldh.	Steroidal	Alvarez et al., 2001 Zamilpa et al., 2002
	Solanum khasianum C.B.Clarke	Steroidal	Putalun et al., 1999
Styracaceae	*Styrax officinalis* L.	Triterpenoid	Yayla et al., 2002
Taccaceae	*Tacca chantrieri* André	Steroidal	Yokosuka et al., 2002b
Ternstroemiaceae	*Camellia sinensis* L. var. *assamica* Pierre	Triterpenoid	Murakami et al., 1999b, 2000b Lu et al., 2000
	Ternstroemia japonica Thunb.	Triterpenoid	Shin et al., 2003
Tiliaceae	*Corchorus depressus* L.	Triterpenoid	Ahmad et al., 2000
Verbenaceae	*Duranta repens* L.	Triterpenoid	Hiradate et al., 1999
Zygophyllaceae	*Fagonia cretica* L.	Triterpenoid	Khalik et al., 2000
	Fagonia indica Burm.f.	Triterpenoid	Shaker et al., 1999
	Tribulus terrestris L.	Steroidal	Xu et al., 2000 Cai et al., 2001 Kostova et al., 2002 de Combarieu et al., 2003
	Zygophyllum decumbens Del.	Triterpenoid	Pöllmann et al., 1998
	Zygophyllum gaetulum Emb. & Maire	Triterpenoid	Safir and Fkih-Tetouani, 1998 Aquino et al., 2001

the typical response in cancer cells, were isolated from the root bark of *Becium grandiflorum* (Lam.) Pichi-Serm. var. *obovatum* (E.Mey. ex Benth) Sebald (Lamiaceae) due to the traditional use of the plant (along with four others) for the treatment of breast and buccal cancer (Burger et al., 1998). A further 10% of the species listed were selected based on previous ethnobotanical studies on related species either of the same genus or family. *Allium nutans* L. (Alliaceae), a wild species of onion, was investigated because of the many reports on the steroidal saponins from *Allium* species (Akhov et al., 1999). This approach to drug discovery has received renewed interest in recent years, and potentially increases the chances for the discovery of novel therapeutic agents (Fabricant and Farnsworth, 2001).

As mentioned earlier, steroidal saponins are almost exclusively found in the monocotyledonous angiosperms. This trend is confirmed by the presence of steroidal saponins in the monocotyledonous families of the Agavaceae, Alliaceae, Asparagaceae, Dioscoreaceae, Dracaenaceae, Liliaceae and Taccaceae. Interestingly, although the family Solanaceae is dicotyledonous, all the species studied contained steroidal saponins. Other exceptions include the presence of steroidal saponins in *Aspilia montevidensis* (Asteraceae), *Balanites aegyptiaca* (Balanitaceae), *Trigonella foenum-graecum* (Leguminosae) and *Tribulus terrestris* (Zygophyllaceae).

Eighteen species of the family Araliaceae have been extensively investigated, as seen in Table 1, five of which are from the genus *Panax*. Species of *Panax* (ginseng) have been known to contain saponins for centuries, however, recent studies on ginseng saponins have investigated their biological activities (Huong et al., 1998b; Kim et al., 1998b; Kim and Kim, 1999; Tran et al., 2001a, 2002; Liao et al., 2002; Zou et al., 2002a; Yoshikawa et al., 2003). The Leguminosae have also been extensively investigated for saponins, in particular, species of *Acacia*, *Albizia* and *Astragalus*. Table 1 lists 23 species of the Leguminosae from which saponins have been isolated.

4. Conclusion

Saponins are a diverse family of secondary metabolites produced by many plants species. Many plants used in traditional medicine worldwide contain saponins, which can often account for there therapeutic action. It is believed that the natural role of these compounds in plants is to protect against attack by potential pathogens, which would account for their antimicrobial activity (Osbourn, 2003). Although saponins are extremely toxic to cold-blooded animals, their oral toxicity to mammals is low (Dini et al., 2001a, 2001b). Due to their toxicity to various organisms, saponins can be utilised for their insecticidal, antibiotic, fungicidal, and pharmacological properties. The wide chemical diversity of both triterpenoid and steroidal saponins has resulted in renewed interest and investigations of these compounds in recent years, particularly as potential chemotherapeutic agents. This review, and the list of species presented in Table 1, provides a summary of saponin research in the last 5 years. It highlights important areas of research in this field, and the opportunity which exists for further research on the phytochemistry and biological activity of this group of compounds. Balandrin et al. (1993) estimate that at least 85% of the world's estimated 250 000 species of higher plants have not been adequately surveyed for potentially useful biological activity. As a result, the chances of discovering new plant constituents, including novel saponins, which may be biologically active are promising.

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